

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 28, 29 and 76 to 80 are pending in the application, with claim 28 being the sole independent claims. Claims 1-27 and 30-75 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Amendment to claim 28 is sought. New claims 76 to 80 are sought to be added. These amendments are supported by the specification and original claims as filed including, *inter alia*: original claims 7, 28; Figure 1, Examples 1, 2 and 3; and paragraphs [0018], [0020], [0025], and [0050] as numbered in the published patent application. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Withdrawal of Claims

The Examiner has withdrawn claims 1-27 and 30-75 from further consideration as being drawn to nonelected inventions. Office Action at page 2. Solely to advance prosecution, and not in acquiescence to the Examiner's argument, Applicants have cancelled claims 1-27 and 30-75, rendering moot the Examiner's grounds for objection.

Priority

The Examiner has asserted that:

[Applicants have] not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 [because a]n application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification [and p]riority is claimed to application 10/019,153 filed 12/21/01, the same day the instant application was filed. Consequently the '153 application is not a prior application under 35 U.S.C. 120, and the priority claim to the '153 application is improper.

Office Action at pages 2-3. Applicants respectfully disagree. 35 U.S.C. § 365(c) states:

(c) In accordance with the conditions and requirements of section 120 of this title, an international application designating the United States shall be entitled to the benefit of the filing date of a prior national application or a prior international application designating the United States, and a national application shall be entitled to the benefit of the filing date of a prior international application designating the United States.

Thus, under 35 U.S.C. § 365(c), the *filing date of the U.S. National Phase is the filing date of the International Application*. As is clearly stated in the cross reference to related applications in the present specification, U.S. Application No. 10/019,153 is the *U.S. National Phase* of International Application PCT/GB00/02459. Therefore, the filing date of U.S. Application No. 10/019,153 is June 23, 2000, which is clearly prior to the December 21, 2001, filing date of the present application.

Furthermore, Applicants followed USPTO practice in claiming the benefit of priority. MPEP § 201.11 recites:

Where a nonprovisional application is claiming the benefit under 35 U.S.C. 120 of a prior national stage application under 35 U.S.C. 371, a suitable reference would read "This application is a continuation of U.S. Application No. 08/---, ** which was the National Stage of International Application No. PCT/DE95/---, filed ---."

Applicants have therefore made a proper claim of benefit of priority. The Examiner's objection is in error. Applicants respectfully request that the Examiner withdraw the objection.

Information Disclosure Statement

The Examiner has objected to the Information Disclosure Statement filed May 20, 2002, alleging that:

[it] fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood . . . of each patent that is not in the English language. It has been placed in the application file, but the information referred to therein as reference AN2, EP 0590530 has not been considered.

References AP1, WO 92/22644, and AR1, Brignon et al., were considered only so far as the contents of their English abstracts, the remainder of these references not being in English.

Office Action at pages 3-4. Applicants respectfully disagree with the Examiner's grounds for objection to the Information Disclosure Statement.

Under MPEP § 609 III (A)(3), "[s]ubmission of an English language abstract of a reference may fulfill the requirement for a concise explanation." The unverified English language abstract appearing on the face of each of Documents AP1 and AR1 is sufficient to comply with the requirements of 37 C.F.R. § 1.98, as it provides a concise explanation of the relevance of the document as understood by Applicants' representative. In a similar manner, the unverified English language abstract submitted as Document AT12 is sufficient to comply with the requirements of 37 C.F.R. § 1.98, as it provides a concise explanation of the relevance of Document AN2, as understood by Applicants' representative. In fact, the Examiner has initialed the Form PTO-1449 listing of

Document AT12, indicating that he has considered the unverified English language abstract for Document AN2.

Under 37 C.F.R. § 1.97(b) "An information disclosure statement *shall* be considered by the office if filed [in accordance with 37 C.F.R § 1.98 and other requirements of 37 C.F.R § 1.97]" (emphasis added). Accordingly, if a non-English language document is provided along with a concise explanation of its relevance, the Examiner shall consider the document. Each of Documents AP1, AR1 and AN2 were accompanied by an unverified English language abstract. The Examiner initialed the Form PTO-1449 indicating that Documents AP1, AR1 and AT12 were considered. Applicants therefore respectfully submit that the concise explanation of Document AN2 required under 37 C.F.R. § 1.98(a)(3) has not only been made of record, but has also been considered by the Examiner. Applicants thus request that the Examiner consider Document AN2 and appropriately initial Form PTO-1449, in accordance with 37 C.F.R § 1.97, and that an Examiner-initialed copy of this Form PTO-1449 evidencing consideration of Document AN2 be included with the Examiner's next communication to Applicants.

Objections to the Drawings

The Examiner has objected to the Drawings because the four sheets of Figure 2 were not numbered in accordance with 37 C.F.R. § 1.84 (u)(1). Applicants thank the Examiner for bringing this informality to their attention. In accordance with 37 C.F.R.

§ 1.84, Applicants submit herewith corrected drawings numbered as Figures 2A, 2B, 2C and 2D, and also amend the specification to make reference to the renumbered drawings. Thus, the Examiner's objection has been accommodated.

Objection to the Specification

The Examiner has objected to the specification, stating that "the nucleotide and amino acid sequences shown in Fig. 1 are not identified by the assigned SEQ ID NO, as required by 37 C.F.R 1.821(d)." Office Action at page 4. As suggested by the Examiner, Applicants have amended herewith the "Brief Description of the Drawings" to include reference to the assigned SEQ ID NOs for the sequences shown in Figure 1. Thus, the Examiner's objection has been accommodated.

Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 112, first paragraph, alleging:

the specification, while being enabled for a transgenic non-human placental mammal wherein the DNA molecule is operably linked to a promoter of a gene encoding a naturally derived milk protein, such that when the mammal is lactating, the fusion protein is preferentially expressed in its mammary tissue and secreted into its milk, does not reasonably provide enablement for any other embodiment embraced by the claims.

Office Action at page 5. Applicants respectfully disagree.

In alleging that the breadth of the claims is not enabled by the specification, the Examiner states that the claims embrace a "DNA molecule [which] is expressed in mammary tissue of female mammals during lactation, whether expressed in milk or not."

Office Action at page 5. Applicants note that in the present specification, transgenic *male* rabbits have been shown to be capable of being induced to produce fusion protein from mammary glands. *See* Example 2. Applicants also note that lactation may not be necessary. The specification states that:

[a] DNA sequence which is suitable for directing the production to the milk of transgenic animals carries a 5' promoter region derived from a naturally derived milk protein and is consequently under the control of hormonal and tissue specific factors. Such a promoter is therefore most active in lactating mammary tissue.

Published Application at paragraph [0050]. Thus, while maximal expression may be observed in the milk of lactating animals, expression is not necessarily limited to lactating mammary tissue. As one of ordinary skill in the art would appreciate, expression from such a gene construct might be expected to be somewhat "leaky", *i.e.* a low level of expression might occur even in non-lactating mammary tissue. In any event, the present claims specify that the encoded fusion protein is produced in the milk of the claimed transgenic mammal, thus rendering moot this portion of the rejection.

In alleging that the breadth of the claims is not enabled by the specification, the Examiner further states that "[t]he only disclosed end use for the claimed transgenic non-human mammal is for the production of the fusion protein in milk of a lactating female animal for subsequent isolation of the peptide." Office Action at page 5. Applicants respectfully disagree, and assert that protein expression in milk is not the only utility for the claimed transgenic animals. For example, animals made by the disclosed methods could carry the transgene in their germline, and such transgenic animals would then be suitable for breeding to produce progeny transgenic animals that carry the transgene and produce the fusion protein. Indeed, this very utility is disclosed in the present

specification, *e.g.* at paragraphs [0020] and [0053] in the published application.

Therefore, the Examiner is incorrect in contending that the only utility for the claimed transgenic animals would be to produce the fusion protein in the animal's milk.

In any event, in order to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 28 and provide new claims 76 to 80. The presently claimed invention is drawn to transgenic mammals whose genome incorporates a DNA molecule comprising a coding sequence operably linked to a regulatory sequence, wherein the coding sequence comprises a first segment encoding a fusion partner protein which is lysozyme coupled in-frame to a second segment encoding a peptide not naturally found in milk, and wherein the fusion protein is expressed in the milk of the transgenic animal. Hence, the present claims render this portion of the Examiner's rejection irrelevant.

In view of the foregoing remarks, Applicants respectfully contend that the specification as filed fully describes and enables the presently claimed invention. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph are respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 112, second paragraph, alleging that "[c]laims 28 and 29 are indefinite for recitation in claim 28 of 'coding sequence having a first segment encoding a fusion partner protein . . . coupled to a second segment encoding a peptide.' It is unclear what the coding sequence encodes." Office Action at page 6.

Applicants have amended claim 28 such that it recites that the coding sequence comprises a first segment encoding a fusion partner protein which is lysozyme coupled in-frame to a second segment encoding a peptide. Accordingly, the metes and bounds of the presently claimed invention are defined. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 102 over four cited references. First, the Examiner rejected claim 28 and 29 under 35 U.S.C. § 102(a) as being anticipated by Akinbi *et al.* which, it is alleged, "[discloses] a transgenic mouse whose genome comprises a DNA encoding a fusion protein comprising rat lysozyme fused to a peptide, residues 278-381 of human SP-B." Office Action at page 7. The Examiner also rejected claim 28 and 29 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,993,809 to Weaver *et al.* which, it is alleged, "discloses a transgenic mouse whose genome comprises a DNA encoding a fusion protein comprising rat lysozyme fused to a peptide from human SP-B." Office Action at page 8.

Applicants respectfully traverse this rejection. However, solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 28 and provide new claims 76-80. The presently claimed invention is drawn to a transgenic non-human placental mammal whose genome incorporates a DNA sequence encoding a fusion protein that is expressed in the milk of the transgenic mammal. Neither Akinbi *et al.* nor Weaver *et al.* disclose a transgenic mammal which

expresses a fusion protein into its milk. Accordingly, neither Akinbi *et al.* nor Weaver *et al.* anticipate the presently claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 that are based on these two references.

The Examiner next rejected claims 28 and 29 under 35 U.S.C. § 102(b) as being anticipated by Lee *et al.* which, it is alleged, "discloses a transgenic mouse whose genome comprises a DNA encoding a fusion protein comprising rat lysozyme fused to a peptide, the signal sequence of bovine β -casein." Office Action at page 8. Applicants respectfully traverse this rejection.

As an initial matter, Applicants note that they have claimed the benefit of the filing date of U.K. patent application GB 9914733.2, which was filed June 23, 1999. Lee *et al.* was published July 1998, *i.e.* less than 1 year prior to the priority date of the GB 9914733.2 patent application to which the present patent application is entitled. Accordingly, Lee *et al.* cannot be used to support a rejection of the presently claimed invention under 35 U.S.C. § 102(b).

In any event, solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 28 and provide new claims 76 to 80. The presently claimed transgenic animals comprise a coding sequence which comprises a first segment encoding a fusion partner protein which is lysozyme coupled in-frame to a second segment encoding a peptide not naturally found in milk, and wherein the fusion protein is expressed in the milk of the transgenic animal. In contrast, Lee *et al.* do not show expression of a fusion protein into the milk of the transgenic animal. Indeed, Lee *et al.* do not demonstrate protein expression at all. Lee *et al.* also do

not disclose the expression of a fusion protein comprising lysozyme linked to a peptide that is not naturally found in milk. Accordingly, for each reason, Lee *et al.* do not anticipate the presently claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 that are based on this reference.

Finally, the Examiner rejected claims 28 and 29 under 35 U.S.C. § 102(b) as being anticipated by WO 93/25567 to Deboer *et al.* which, it is alleged, "discloses a transgenic mouse whose genome comprises a DNA encoding a fusion protein comprising rat lysozyme fused to a peptide, the signal sequence of bovine α S1-casein." Office Action at page 8. Applicants respectfully traverse this rejection.

However, solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 28 and provide new claims 76 to 80. The presently claimed transgenic animals comprise a coding sequence which comprises a first segment encoding a fusion partner protein which is lysozyme coupled in-frame to a second segment encoding a peptide not naturally found in milk, and wherein the fusion protein is expressed in the milk of the transgenic animal. In contrast, Deboer *et al.* do not show a transgenic animal which expresses, into its milk, a fusion protein comprising lysozyme linked to a peptide that is not naturally found in milk. Accordingly, Deboer *et al.* do not anticipate the presently claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 that are based on this reference.

For at least the foregoing reasons, the presently claimed invention is not anticipated by the cited references. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Amendments to the Drawings

In the drawings, please substitute the four pages of Figure 2 with four pages of replacement sheets numbered Figures 2A, 2B, 2C and 2D, submitted herewith.